Claudio A. Hetz, Ph.D.

GENERAL INFORMATION

Born March 24, 1976 in Chile
Country of Citizenship: Chile

Principal investigator
Laboratory of Cellular Stress and Biomedicine
Institute of Biomedical Sciences
Faculty of Medicine, University of Chile
1027 Independencia. POBox 70086
Santiago, Chile
Phone: 56-2-9786506 (office); FAX: 56-2-9786871
email: chetz@med.uchile.cl and chetz@hsph.harvard.edu
Websites: www.hetzlab.cl
or: www.bni.cl, www.cmcmed.cl, www.neurounion.com,
http://www.hsph.harvard.edu/claudio-hetz/

IMPACT

Total citations (ISI Web of Knowledge): **5500**
H-Factor: **36**

Personal statement

This laboratory focuses on understanding the molecular basis of organelle stress and its relationship to pathological conditions affecting the nervous system, and the development of prototypic therapies to prevent this damage. Our laboratory is committed to the study of cellular strategies involved in adaptation to chronic endoplasmic reticulum (ER) stress. The ER has important cellular functions, highlighting its role as sophisticated machinery for protein folding and secretion. ER stress engages an integrated signaling pathway known as the "Unfolded Protein Response" (UPR), which aims to restore homeostasis. Nevertheless, the mechanisms that control the transition from an adaptive state to cell death processes remain unknown and is a central subject of our research. We are currently developing a systematic approach to underscore the effects of targeting the UPR in several brain diseases involving protein misfolding using genetic manipulation of the pathway in mouse models in addition to develop gene therapy strategies to alleviate ER stress. Our laboratory is one of the most productive groups in Chile and supported by various national and international organizations.

EXPERIENCE AND EDUCATION

07/11-present **HARVARD SCHOOL OF PUBLIC HEALTH** **BOSTON, USA**
Department of Immunology and Infectious Diseases
Adjunct Professor

07/11- present **UNIVERSITY OF CHILE** **SANTIAGO, CHILE**
Deputy Director,
Biomedical Neuroscience Institute

03/10- present **UNIVERSITY OF CHILE** **SANTIAGO, CHILE**
Full Professor and Principal Investigator
Institute of Biomedical Sciences

06/10- present **Neurounion Biomedical Foundation /CENPAR** **SANTIAGO, CHILE**
Member of the Director Board

09/09- 2012 **UNIVERSITY OF CHILE** **SANTIAGO, CHILE**
Principal Investigator
FONDAP Center for Molecular Studies of the Cell

11/08- 2010 **UNIVERSITY OF CHILE** **SANTIAGO, CHILE**
Principal Investigator
Millennium Nucleus for Neural Morphogenesis (NEMO)

01/07- 03/10 **UNIVERSITY OF CHILE** **SANTIAGO, CHILE**
Assistant Professor and Principal Investigator
Institute of Biomedical Sciences

01/07- 09/09 **UNIVERSITY OF CHILE** **SANTIAGO, CHILE**
Associate Investigator
FONDAP Center for Molecular Studies of the Cell

05/08-07/11 **HARVARD SCHOOL OF PUBLIC HEALTH** **BOSTON, USA**
Department of Immunology and Infectious Diseases
Adjunct Assistant Professor

08/05-12/07 **HARVARD SCHOOL OF PUBLIC HEALTH** **BOSTON, USA**
Department of Immunology and Infectious Diseases
Postdoctoral Research Fellow
Regulation of the Unfolded Protein Response in the CNS.
Advisor: Laurie H. Glimcher, M.D.

08/04-08/05 **DANA-FARBER CANCER INSTITUTE** **BOSTON, USA**
HOWARD HUGHES MEDICAL INSTITUTE
HARVARD MEDICAL SCHOOL
Department of Cancer Immunology & AIDS
Postdoctoral Research Fellow
Regulation of apoptosis by the BCL-2 protein family.
Advisor: Stanley Korsmeyer, M.D.

01/02-07/04 **SERONO PHARMACEUTICAL RESEARCH INST.** **GENEVA, SWITZERLAND**
Department of Neurobiology
PhD. In Biomedical Sciences, doctoral thesis: "The role of the Unfolded Protein Response and Endoplasmic Reticulum Stress in Prion-related disorders".
Advisor: Claudio Soto, Ph.D.

03/00-12/01 **UNIVERSITY OF CHILE** **SANTIAGO, CHILE**
Faculty of Medicine, Institute of Biomedical Sciences
Residence of Ph.D.
Study of Fas signaling in lymphoid cells involved in non-apoptotic cell death.
Advisor: Andrew Quest, Ph.D.

03/95-03/00 **UNIVERSITY OF CHILE** **SANTIAGO, CHILE**
Faculty of Sciences
Degree *of Molecular Biotechnology Engineer*. Degree thesis: "Cytotoxic mechanism of the bacterial forming-channel Microcin E492 in human carcinoma cells". Advisors: Rosalba Lagos, Ph.D. and Maria R. Bono, Ph.D.

HONORS, AWARDS AND FELLOWSHIPS

2015	**KIA International Award** (KIA) Laureate, first place, for invaluable achievements and contributions to the development of science and technology. In addition, this price was accompanied by an **UNESCO special award**.
2014	Selected by the LatinAmericanScience.Org and *Qué Pasa* magazine as one of the 30 more influencing scientist in Latin America.
2014	Target Validation Award, Michael J Fox Foundation for Parkinson Research, USA.
2014	Frick Foundation Award, Switzerland. Received one of the two international arads for ALS research.
2012	Awarded with the **FEBS Anniversary Prize** of the Gesellschaft für Biochemie und Molekularbiologie. IUBMB & FEBS meeting, Sevilla, Spain.
2012	Awarded with a gift from the Christopher Reeve Spinal Cord Injury and Paralysis Foundation, USA.
2011	Young investigator Awards, **North American Spine Society**, USA.
2010	Selected by the Latin-American Science Academy to represent Chile in the IAP Young Scientists Conference organized in conjunction with the World Economic Forum in China.
2009	Selected on a study form the Ministry of Economy of Chile as one of the successful stories in innovation and Science in Chile.
2008	Awarded with the **Young Scientist Prize TWAS-ROLAC** from the Latin-American Science Academy for the best young scientist in the region and the Caribbean.
2008	**The Eppendorf & *Science* Prize for Neurobiology**, selected finalist by the editors of Science magazine as outstanding young scientist.
2008	Awarded with the "**Cell Biology Society and Bios-Chile prize**" as the best young scientist of Chile.
2008	Angel Fund Junior Investigator Award for Outstanding Research, Sporadic Neurodegeneration: Genes, Environment and Therapeutic Strategies. Boston, USA.
2008	Member of The Cell Biology Society of Chile.
2007	Selected by the newspaper "El Mercurio" as one of *the 100 Chilean young leaders 2007*.
2007	Awarded with a High Q Foundation Discovery Initiative Research grant
2004-2007	**Damon Runyon Cancer Research**. Research fellowship for postdoctoral training in Stanley Korsmeyer's laboratory at Dana-Farber Cancer Institute, Harvard Medical School, Boston, USA.
2004-2007	Cancer Research Institute. Research fellowship for postdoctoral training in Stanley Korsmeyer's laboratory at Dana-Farber Cancer Institute, Harvard Medical School, Boston, USA (withdraw of candidature to accept previous fellowship).
2003	Member of the Society of Neuroscience, USA.
2003	**Herman Neimeyer Medal**, Chilean Society of Biochemistry and Molecular Biology. Recognition as the best Ph.D. student in Biomedical Sciences of Chile, 2003.
2002-2004	**Federal Swiss Confederation Scholarship** for Ph.D. thesis at Serono Pharmaceutical Research Institute, Geneva, Switzerland.
2002	CONICYT fellowship (Chilean Government) for Ph.D. studies.
2001	Traveling Fellowship from the I.C.B.M., University of Chile, to perform a research steady at the Institute of Biochemistry, University of Lausanne, Switzerland, and at N.C.I, Washington, USA
2000-2001	**Fundación Andes** fellowship for Ph.D. studies in Biomedical Sciences.
2000	Honor with Maximum Distinction and fist degree in generation 2000, Molecular Biotechnology Engineer, University of Chile.

PUBLICATIONS, REVIEWS, EDITORIAL COMMENTS, AND BOOK CHAPTERS
*Publications with affiliation to the University of Chile
#Corresponding author

1. **Hetz C**., Chevet E., and Oakes S. (2015). Proteostasis control by the unfolded protein response. ***Nature Cell Biology.*** 7:829-38.*#

2. Torres M, Medinas DB, Matamala JM, Woehlbier U, Cornejo VH, Solda T, Andreu C, Rozas P, Matus S, Muñoz N, Vergara C, Cartier L, Soto C, Molinari M, **Hetz C.** (2015). The Protein Disulfide Isomerase ERp57 Regulates the Steady-State Levels of the Prion Protein. ***J Biol Chem***. *In press*.*#

3. Rojas-Rivera D. and **Hetz C**. (2015). TMBIM protein family: ancestral regulators of cell death. ***Oncogene***. 34:269-280.*#

4. Garcia-Huerta P., Rivas A., **Hetz C.** (2015) Stressing out the ER in aminoglycoside-induced hearing loss. ***Cell Death Dis.*** 14;6:e1762. **Editorial comment**. *#

5. Cardenas-Sureda A. and **Hetz C.** (2015) RNA metabolism: Putting the brake on the UPR. ***EMBO Rep.*** 6:545-6. **Editorial comment**. *#

6. **Hetz C.** and Chevet E. (2015) Theme Series - UPR in cancer. ***Sem Cancer Biology.*** 33:1-2. Editorial comment. *#

7. Chevet E., **Hetz C.**, Samali A. (2015) Endoplasmic Reticulum Stress-Activated Cell Reprogramming in Oncogenesis. ***Cancer Discovery.*** 5:586-97*

8. Dufey E., Urra H., and **Hetz C**. (2015). ER proteostasis addiction in cancer biology: Novel concepts***. Sem Cancer Biology.*** 33:40-7*#

9. Gonzalez-Perez P., Woehlbier U., Chian RJ., Sapp P., Rouleau GA., Leblond CS., Daoud H., Dion P.A, Landers J.E., **Hetz C.**, Brown R.H. (2015). Identification of rare protein disulfide isomerase gene variants in amyotrophic lateral sclerosis patients, ***Gene***. 566:158-65. *#

10. Mercado G., Castillo V., Vidal R. and **Hetz C.** (2015) ER proteostasis disturbances in Parkinson's disease: novel insights. ***Frontiers Aging Neurosci.*** 7:39. *#

11. Torres M., Matamala J.M., Duran-Aniotz C., Cornejo V.H., Foley A., **Hetz C**. (2015) ER stress signaling and neurodegeneration: At the intersection between Alzheimer's disease and Prion-related disorders. ***Virus Res***. pii: S0168-1702(14)00523-1. *#

12. Rivas A., Vidal R. and **Hetz C**. (2015) Pharmacological strategies to target endoplasmic reticulum (ER) stress with chemical and natural compounds***. Expert Opinion Therapeutic Targets***. 13:1-16. ***#**

13. Mercado G., Castillo V. and **Hetz C**. (2015) Mercado G., Gene therapy in Parkinson´s disease: targeting the ER proteostasis network. ***Neural Regeneration Research.*** *In press*. ***#**

14. **Hetz C.** and Mollereau B. (2014) Disturbance of ER proteostasis in neurodegenerative diseases. ***Nature Rev Neurosci.*** 15:233-249.*#

15. Valdés P., Mercado G., Vidal R., Parsons G., Court F., Molina C., Martinez A., Galleguillos D., Armentano D., Schneider B., and **Hetz C.** (2014). Control of dopaminergic neuron survival by the unfolded protein response transcription factor XBP1. ***Proc Natl. Acad. Asci USA.*** 111:6804-9. *#

16. Groenendyk J., Peng Z., Dudek E., Fan X., Mizianty M., Dufey E., Urra H., Sepulveda D., Rojas-Rivera D., Lim Y., Han Kim D., Baretta K., Srikanth S., Gwack Y., Ahnn J., Kaufman K., Lee S., **Hetz**

C., Kurgan L. and Michalak M. (2014) Interplay Between the Oxidoreductase PDIA6 and microRNA-322 Controls the Response to Disrupted Endoplasmic Reticulum Calcium Homeostasis. ***Science Signaling*** 7: 1-14.* (**Cover illustration)**

17. Nassif M., Valenzuela V., Rojas-Rivera D., Vidal R., Matus S, Castillo K., Fuentealba Y., Kroemer G., Levine B., and **Hetz C**. (2014) Pathogenic role of BECN1/Beclin 1 in the development of amyotrophic lateral sclerosis. ***Autophagy.*** 10: 1256-1271*#. (**Cover illustration)**.

18. Urra H. and **Hetz C.** A novel ER stress-independent function of the UPR in angiogenesis. ***Mol Cell.*** 54:542-544. **Editorial comment**. *#

19. Medinas D. and Hetz C. (2014) Protein folding stress: Modeling UPR adaptive responses. ***Nature Chem Biol.*** 10:879-80. **Editorial comment**. *#

20. Mardones P. Martinez G., and **Hetz C**. (2014) Control of systemic proteostasis by the nervous system. ***Trends Cell Biol.*** 25:1-10*#. (**Cover illustration)**.

21. Vidal R., Matus S., Bargsted L., and **Hetz C**. (2014) Targeting autophagy in neurodegenerative diseases***. Trends Pharmacol Sci.*** 35: 583-91*# (**Cover illustration)**.

22. Couve A. and **Hetz C.** (2014) RESETing ER proteostasis: New stress pathways hidden in the secretory pathway. ***EMBO J.*** 33:2444-6. **Editorial comment**. *#

23. Matus S., Bosco D., and Hetz C. (2014) Autophagy meets FUS-positive Stress Granules. ***Neurobiol Dis***. 35: 2832-5. **Editorial comment**. *#

24. Dufey E., Sepulveda D., Rojas DR., and **Hetz C**. (2014). ER stress signaling mechanisms: an overview. ***Am J. Physiol -Cell Physiology***. 307:C582-94. *#

25. Mardones P., Dilllin A. and **Hetz C.** (2014). Cell-nonautonomous control of the UPR: Mastering energy homeostasis. ***Cell Metabolism***. 20:385-7. **Editorial comment**. *#

26. Matus S., Medinas D., and **Hetz C.** Common Ground: Stem Cell Approaches Find Shared Pathways Underlying ALS. ***Cell Stem Cell.*** 14: 697-699. **Editorial comment**. *#

27. Torres M, Matamala JM, Duran-Aniotz C, Cornejo VH, Foley A, **Hetz C**. (2014) ER stress signaling and neurodegeneration: At the intersection between Alzheimer's disease and Prion-related disorders. ***Virus Res***. 2014 Dec 31. pii: S0168-1702(14)00523-1. *#

28. Campos G., Schmidt-Heck W., Ghallab A., Rochlitz K., Pütter L., Medinas D., **Hetz C.**, Widera A, Cadenas C, Begher-Tibbe B., Reif R., Günther G., Sachinidis A., Hengstler J., and Godoy P. (2014) The transcription factor CHOP, a central component of the transcriptional regulatory network induced upon CCl4 intoxication in mouse liver, is not a critical mediator of Hepatotoxicity. ***Archives Toxicol***. 88: 1267-1280.*

29. Dejeans N., Manié S., **Hetz C.**, Bard F., Hupp T., Agostinis P., Samali A. and Chevet E. (2014). Addicted to secrete – novel concepts and targets in cancer therapy. ***Trend Mol Med.*** 20: 242-250.*

30. Duran-Aniotz C., Martinez G. and **Hetz C.** (2014) Memory loss in Alzheimer´s disease: Are the alterations in the UPR network involved in the cognitive impairment? ***Frontiers Aging Neurosci.*** 6:1-3.*#

31. Matus S., Valenzuela V. and **Hetz C**. (2014). A new method to measure of autophagy flux in the nervous system. ***Autophagy.*** 10:710–714.*#

32. **Hetz C**. (2013). The biological meaning of the UPR. ***Nature Rev Mol Cell Biol***. 14:404. **Journal Club** [*#]

33. **Hetz C.**, Chevet E., and Harding H. (2013). Targeting the unfolded protein response in disease. ***Nature Rev Drug Discovery*** 12:703-719. [*#]

34. Vilches D. and **Hetz C.** (2013). Proteostasis impairment: A molecular intersection between Alzheimer´s disease and diabetes. ***Cell Metabolism.*** 8:771-2. **Editorial comment**. [*#]

35. Acuña A., Esparza M., Kramm C., Beltrán F., Parra A., Cepeda C., Toro C., Vidal R., **Hetz C.**, Concha I., Brauchi S., Levine M. and Castro M. (2013) A failure in energy metabolism and antioxidant uptake precede the onset of Huntington's disease. ***Nature Communications.*** 13:2917.*

36. Castillo K., Valenzuela V., Matus S., Nassif M., Oñate M, Fuentealba Y. Encina G., Irrazabal T., Parsons G., Court F., Schneider B., Armentano D., and **Hetz C.** (2013) Measurement of autophagy flux in the nervous system *in vivo.* ***Cell Death Dis.*** 4:e917. [*#]

37. Castillo K., Nassif M., Valenzuela V., Rojas F., Matus S., Mercado G., Court F., van Zundert B., and **Hetz C.** (2013) Trehalose delays the progression of amyotrophic lateral sclerosis by enhancing autophagy in motoneurons. ***Autophagy*** 9:1308-20. [*#]

38. Matus S, Lopez E., Valenzuela V., Nasiff M., and **Hetz C.** (2013) Functional role of the transcription factor ATF4 in the pathogenesis of amyotrophic lateral sclerosis. ***PloS One*** 8:e66672.

39. Hurra H, Dubey E, Lisbona F, Rojas D, and **Hetz C**. (2013). When ER stress reaches a dead end. ***Biochim Biophys Acta (BBA) - Molecular Cell Research***. S0167-4889(13)00311-X. [*#]

40. Kiviluoto S., Luyten T., Schneider L., Lisak D., Rojas-Rivera D., Welkenhuyzen K., Missiaen L., De Smedt H., Parys J., **Hetz C.**, Methner A., Bultynck G. (2013) Bax Inhibitor-1-mediated Ca2+ leak is decreased by cytosolic acidosis. ***Cell Calcium***. 54:186-192. [*]

41. Mercado G., Valdés P., and Hetz C. (2013) An ERcentric view of Parkinson's disease. ***Trends Mol. Med***. 19(3):165-75. [*#]

42. Quiroga C., Gatica D., Paredes F., Bravo R., Troncoso R:, Pedrozo Z., Rodriguez A., Vicencio J.M., Toro B., Chiong M., **Hetz C** and Lavandero S. (2013) Herp depletion protects from ***Biochim Biophys Acta. (BBA) - Molecular Cell Research***. 1833:3295-3305. [*#]

43. Vidal R. and **Hetz C**. (2013). Unspliced XBP1 controls autophagy through FoxO1. ***Cell Res.*** 23(4):463-4. **Editorial comment**. [*#]

44. Matus S., Valenzuela V., Medina D. and **Hetz C** (2013). ER dysfunction and protein folding stress in ALS. ***Int. J Cell Biol.*** 2013:674751. [*#]

45. Cornejo VH, Pihán P., Vidal R., and **Hetz C**. (2013). Role of the UPR in organ physiology: Lessons from mouse models. ***IUBMB Life*** 65:962-75. [*#]

46. Cornejo VH. and **Hetz C**. (2013). The Unfolded Protein Response in Alzheimer's disease. ***Semminars Immunol.*** 35(3):277-92. [*#]

47. Smaili SS, Quest AF, **Hetz C**, Lavandero S. (2013) Editorial: signaling in cell death, survival, proliferation and degeneration. ***Curr Mol Med.*** 2013 Feb 1;13(2):239-40 [*#]

48. **Hetz C**. (2012). The unfolded protein response: controlling cell fate decisions under ER stress and beyond. ***Nat Rev. Mol Cell Biol.*** 13(2):89-102. [*#]

49. Rodriguez D., Zamorano S., Lisbona F., Rojas D., Cubillos-Ruiz J., Armisen R., Henriquez D., Urra H., Cheng E., Letek M., Vaisar T., Irrazabal T., Gonzalez-Billault C., Letai A., Pimentel-Muiños F., Kroemer G. and **Hetz C.** (2012). BH3-only proteins are part of a regulatory network that control the sustained signaling of the Unfolded Protein Response sensor IRE1. ***EMBO J.*** 31(10):2322-35.[*#]

50. Vidal R., Figueroa A., Court F., Thielen P., Molina C., Wirth C., Caballero B., Kiffin R., Segura-Aguilar J., Cuervo AM, Glimcher L., and **Hetz C.** (2012). Targeting the UPR transcription factor XBP1 protects against Huntington's disease through the regulation of FoxO1 and autophagy. ***Hum. Mol. Gen.*** 21(10):2245-62. [*#]

51. Rojas-Rivera D, Armisén R., Colombo A., Eguiguren A., Martínez G., Díaz A., Kiviluoto S., Rodríguez D., Patron M., Rizzuto R., Bultynck G., Concha M., Sierralta J., Stutzin A., and **Hetz C**. (2012). TMBIM3/GRINA is a novel Unfolded Protein Response (UPR) target gene that controls apoptosis through the modulation of ER calcium homeostasis. ***Cell Death Diff.*** 9:1013-26. [*#]

52. Zamorano S., Rojas-Rivera D., Lisbona F., Parra V., Court F., Villegas R., Cheng E., Korsmeyer S., Lavandero S., and **Hetz C**. (2012) A BAX/BAK and Cyclophilin D-independent Intrinsic Apoptosis Pathway. ***PLoS One*** :e37782. [*#]

53. Valenzuela V, Collyer E., Armentano D., Parsons G., Court F. and Hetz C. (2012). Activation of the Unfolded Protein Response enhances motor recovery after spinal cord injury. ***Cell Death Dis.*** 3, e272 [*#]

54. Torres M., Cartier L., Matamala J, Hernandez N., Woehvier U., and **Hetz C.** (2012). Altered Prion protein expression pattern in CSF as a biomarker for Creutzfeldt-Jakob Disease. ***PLoS One*** .7:e36159. [*#]

55. Read D., Deepti A., Cawley K., Gupta A., Oommen D., Verfaillie T., Matus S., Agostinis P., **Hetz C.**, Samali A. (2012) Perk-dependent Repression of miR-106b-25 Cluster is Required for ER stress-induced Apoptosis. ***Cell Death Dis.*** 28;3:e333 [*#]

56. Zuleta A., Rene L. Vidal R., Armentano D., Parsons G., and **Hetz C**. (2012). AAV-mediated delivery of the transcription factor XBP1s locally into the striatum reduces mutant Huntingtin aggregation in a mouse model of Huntington's Disease. ***Biochem. Biophys Res Comm***. 13:558-63.[*#]

57. Herrera R., Frischknecht R., Seidenbecher C., Gundelfinger E., **Hetz C.,** Aylwin M., Schneider P., Quest A. And Leyton L. (2012) Astrocytic aVb3 Integrin Inhibits Neurite Outgrowth and Promotes Retraction of Neuronal Processes by Clustering Thy-1. ***PLoS One***. 7: e34295. [#]

58. Martinez G. and **Hetz C.** (2012) Cell-nonautonomous control of the Unfolded Protein Response. ***EMBO Rep***. 13:767-8. **Editorial comment**. [*#]

59. Urra H. and **Hetz C.** (2012). The ER in 4D: A novel stress pathway controlling endoplasmic reticulum membrane remodeling. ***Cell Death Diff.*** 19:1893-5. **Editorial comment**. [*#]

60. Nassif M and **Hetz C** (2012) Autophagy impairment: A crossroad between neurodegeneration and Tauopathies. ***BMC Biology***. 13:767-8 **Editorial comment**. [*#]

61. Klionsky and 1269 (**Hetz C**) others. (2012). Guidelines for the Use and Interpretation of Assays for Monitoring Autophagy in Higher Eukaryotes. ***Autophagy***. 8:445.554. [*#]

62. Vidal R. and **Hetz C**. 2012. Crosstalk between the UPR and autophagy pathway contribute to handling cellular stress in neurodegenerative disease. ***Autophagy***. 8:970-2. [*#]

63. Matus S, Castillo K, and Hetz C. (2012) Hormesis: Protecting neurons against cellular stress in Parkinson´s disease. ***Autophagy***. 8:997-1001.[*#] **Editorial comment**.[*#]

64. Andreau C, Woehlbier U, Torres M, and **Hetz C**. (2012). Protein Disulfide Isomerases in Neurodegeneration: from disease mechanisms to biomedical applications. ***FEBS Lett.*** 586:2826-34.[*#]

65. Castillo K, Rojas-Rivera D., Lisbona F., Caballero B., Nassif M., Court F., Schuck S., Ibar C., Walter P., Sierralta J., Glavic A., and **Hetz C**. (2011). BAX inhibitor-1 regulates autophagy by controlling the IRE1a/JNK branch of the unfolded protein response. ***EMBO J.*** 4465-78[*#]

66. **Hetz C**, Martino F, Rodriguez, and Glimcher LH. (2011). The Unfolded Protein Response: Integrating stress signals through the stress sensor IRE1α. ***Physiological Reviews***. 91:1219-43.[*#]

67. Woehlbier U. and **Hetz C**. (2011). Modulating stress responses by the UPRosome: A matter of life and death. ***Trends in Biochem Ssci (TiBS)***, 36:329-37.[*#]

68. Nassif M. and **Hetz C**. (2011). Targeting autophagy in ALS: a complex mission. ***Autophagy***. 7(4).[*#] **Editorial comment**.

69. Matus S., Glimcher LH., and **Hetz C**. (2011). Protein folding stress in neurodegenerative diseases: a glimpse into the ER. ***Curr Op. Cell Biol.*** 23:239-52.*#

70. **Hetz C.** and Glimcher LH. (2011) Protein homeostasis networks in physiology and disease. ***Curr Op. Cell Biol***. Editorial Overview. 23:123-5. *#

71. Torres M., Encina G., Soto C., and **Hetz C**. (2011). Abnormal calcium homeostasis and protein folding stress at the ER: a common factor in familial and infectious Prion disorders. ***Commun Integr Biol.*** 4: 258 - 261. *#

72. Rodriguez D., Rojas D., and **Hetz C**. (2011). The Endoplasmic Reticulum Gateway of Death. ***Biochimica et Biophysica Acta (BBA) - Molecular Cell Research***. 1813:564-74. *#

73. Barrientos S.A., Martinez N.W., Yoo S., Jara, J.S., Zamorano S, **Hetz, C.**, Twiss J.L. Alvarez J., Court F. A. (2011) Axonal degeneration is mediated by the mitochondrial permeability transition pore. ***J. Neurosci***. 31:966-978. *#

74. Klein A, Maldonado C., Vargas L., Robledo F., Perez de Arce K., Muñoz F., **Hetz C.,** and Alvarez A. (2011). Oxidative stress activates the c-Abl/p73 proapoptotic pathway in Niemann-Pick type C neurons Corresponding ***Neurobiol Dis.*** 41:209-18.

75. Vidal R., Caballero B., Couve A., and **Hetz C**. (2011). Converging pathways in the occurrence of endoplasmic reticulum (ER) stress in Huntington's disease. ***Curr. Mol. Med.*** 11:1-12 (**Cover illustration**) *#

76. Paula-Lima A, T. Adasme, A. Sebollela, **C. Hetz**, M. A. Carrasco, S. T. Ferreira and C. Hidalgo. (2011). Amyloid β peptide oligomers stimulate RyR-mediated Ca2+release inducing mitochondrial fragmentation and prevent RyR-mediated dendritic spine remodeling produced by BDNF in hippocampal neurons. ***Antiox Red Sig***. 14:1209-23.

77. Andres Klein, Matías Mosqueira, Gabriela Martinez, Fermín Robledo, Marcela González, Benjamín Caballero, Gonzalo I. Cancino, Alejandra R. Alvarez, **Claudio Hetz** and Silvana Zanlungo. (2011) Lack of activation of the Unfolded Protein Response (UPR) in mouse and cellular models of Niemann-Pick type C disease. ***Neurodeg Dis***. 8(3):124-8.

78. Sanjeev Gupta, Ayswaria Deepti, Shane Deegan, Fernanda Lisbona, Claudio Hetz and Afshin Samali. (2010). HSP72 Protects Cells from ER Stress-induced Apoptosis via Enhancement of IRE1-XBP1 Signalling through a physical interaction. ***Plos Biology***. 8: e1000410-e1000410.

79. Torres M., Matus S., Arminsen R., Stutzin A., Soto C., and **Hetz C.** (2010). Prion Protein Misfolding Affects Calcium Homeostasis and Sensitizes Cells to Endoplasmic Reticulum Stress. ***PlosOne.*** 5: e15658- e15658.*#

80. Nassif M., Matus S., Castillo K., and **Hetz C.** (2010) Amyotrophic lateral sclerosis pathogenesis: a journey through the secretory pathway. ***Antiox Red. Sig***, 13:1955-89.

81. Matus S., Nassif M., Glimcher LH, and Hetz C. (2009). XBP-1 deficiency in the nervous system revealed a homeostatic switch to activate autophagy. ***Autophagy.*** Nov 6;5(8). (**Cover illustration)** *#

82. **Hetz C.** and Glimcher L. (2009). Fine tuning of the Unfolded Protein Response: Assembling the IRE1 interactome. ***Mol Cell.*** 35:551-61. *#

83. **Hetz C,** Thielen P, Matus S., M Nassif, Court F., Cuervo AM., Martinez G., Kiffin R., R.H. Brown and Glimcher L. (2009). XBP-1 deficiency in the nervous system protects against amyotrophic lateral sclerosis by increasing autophagy. ***Genes & Dev.*** 23:2294–2306. (**Cover illustration)** *#

84. Commented in Genes Dev. (2009), 23:2294-306.

85. Lisbona F. and **Hetz C.** (2009). Turning off the unfolded protein response: An interplay between the apoptosis machinery and ER stress signaling. ***Cell Cycle***. 8:3-4.*#

86. Lisbona F., Rojas D., Thielen P., Zamorano S., Todd D., Martinon F., Glavic A., Kress C.,, Lin J., Walter P., Reed J., Glimcher L. and **Hetz C.** (2009). BAX Inhibitor-1 is a negative regulator of the ER stress sensor IRE1. ***Mol. Cell.*** 33:679-691.*# (**Cover illustration)**

87. Commented in *Mol Cell* (2009), 33:669-70.

88. **Hetz C.** (2009). The UPR as a survival factor of cancer cells: More than folding proteins? ***Leukemia Res.*** 33:880-882.*#

89. Matus S., Lisbona F., Torres M., Leon C., Thielen P., and **Hetz C**. (2008). The stress rheostat: Interplay between the Unfolded Protein Response (UPR) and Autophagy in neurodegeneration. ***Curr. Mol. Med***. 8:157-172. *#.

90. **Hetz C.** (2008). Apoptosis, Autophagy and Necrosis: From mechanisms to biomedical applications. ***Curr. Mol. Med***. 8(2):76-77 *#. Editorial comment.

91. **Hetz C,** Lee AH, Gonzalez-Romero D., Thielen P., Castilla J., Soto C. and Glimcher L. (2008). The Unfolded Protein Response transcription factor XBP-1 does not influence Prion replication or pathogenesis. ***Proc. Natl. Acad Sci.*** 105: 757-62 *#

92. **Hetz C.** and Glimcher L. (2008) The deadly job of night Killer: New regulatory roles of the BCL-2 family in organelle physiology. ***Trends in Cell Biol.*** 18: 38-44 *#. (**Cover illustration)**

93. **Hetz C.** and Glimcher L. (2008). The UPRosome and XBP-1: mastering secretory cell function. ***Curr. Immunol Rev.*** 4:1-10*#.

94. Steele A., **Hetz C.**, Yi C., Jackson W., Borkowski A., Yuan J., Wollmann R., and Lindquist S. (2007). Prion pathogenesis is independent of Caspase-12. ***Prion.*** 4:1-5. *#

95. Steele A., King O., Jackson W., **Hetz C**., Borkowski A., Thielen P., Wollmann R., and Lindquist S. (2007). Diminishing apoptosis by deletion of Bax or overexpression of Bcl-2 does not protect against infectious prion toxicity in vivo (2007) ***J. of Neuroscience***. 27: 13022-7. *

96. **Hetz C.** (2007). ER stress signaling: Form adaptation to irreversible cellular damage. ***Antiox Redox Signal.*** 9:1-12. *#

97. **Hetz C.** Thielen P., Fisher J., Pacinelli, P., Brown, R., Korsmeyer S. and Glimcher L. (2007). The Pro-apoptotic BCL-2 Family Member BIM Mediates Motoneuron Loss in a Model of Amyotrophic Lateral Sclerosis. ***Cell Death and Diff.*** 14(7):1386-1389.*#

98. **Hetz, C**., Castilla, J. and Soto C. (2007). Perturbation of endoplasmic reticulum homeostasis facilitates prion replication. ***J. Biol. Chem.*** 282:12725-33. *#

99. **Hetz, C,** Bernasconi, P., Fisher, J., Lee, A., Bassik, M., Antonsson, B., Brandt, G., Iwakoshi, N,. Schinzel, A., Glimcher, L. and Korsmeyer, S. (2006). Proapoptotic BAX and BAK modulate the unfolded protein response by a direct interaction with IRE1alpha. ***Science.***312: 572-6. #

100. Commented in *Nat. Rev. Cell Biol.* (2006) 7:388 Handling the stress; *ACS Chem. Biol.* (2006) 1:188. Stressed out cells.

101. **Hetz, C.** and Soto, C. (2006). Emerging roles of the Unfolded protein response signaling in physiology and disease. ***Curr. Mol. Med.*** 6: 1-3. Editorial comment as executive editor.*#

102. **Hetz, C.** and Soto, C. (2006). Stressing out the ER: A Role of unfolded protein response in prion-related disorders ***Curr. Mol. Med.*** 6:37-43.*#

103. **Hetz, C.,** Vitte, P., Bombrun, A., Rostovtseva, T., Montessuit, S., Hiver, A., Schwarz, M., Church, D., Korsmeyer, S., Martinou, J.C. and Antonsson, B. (2005). Bax channel inhibitors prevent cytochrome *c* release from mitochondria and protect neurons in a model of global brain ischemia***. J. Biol. Chem.*** 280: 42960-42970.*

104. **Hetz, C**., Torres, V., and Quest A. (2005). Beyond apoptosis: Non-apoptotic cell death in physiology and disease. ***Biochem. Cell. Biol****.* 83:579-588.*

105. Schinzel, A., Takeuchi, O., Huang, Z., Fisher, J., Zhou, Z., Rubens J., **Hetz, C.** Danial, N., Moskowits, M., and Korsmeyer, S. (2005). Cyclophilin D is an essential component of mitochondrial permeability transition and mediates neuronal cell death after focal cerebral ischemia. ***Proc. Natl Acad. Sci. U.S.A.*** 102:12005-12010.

106. Castilla, J., Saa, P., **Hetz, C**. and Soto, C. (2005). In vitro generation of infectious scrapie prions. ***Cell.*** 121:195-206.*

107. Commented in *Cell* (2005) 121:155-162. From microbes to prions: The final proof of the prion hypothesis; *Science* (2005) 421:3. Proof positive for prions; *Nature* (2005) 432:39. Prion progress; *Nature Med.* (2005) 11:480. Nothing but prion.

108. **Hetz C.**, Russelakis, M., Wälchli S., Carboni S., Vial-Knecht E., Maundrell K. and Soto, C. (2005). The disulfide isomerase Grp58 is a protective factor against prion neurotoxicity. ***J. Neurosci***. 25:2793-2802.*

109. Russelakis, M., **Hetz C.**, Maundrell K., and Soto, C. (2004). Prion replication alters the distribution of synaptophysin and caveolin 1 in neuronal lipid rafts. ***Am. J. Pathol****.* 165:1839-1848.*

110. Castilla C., **Hetz C**., Soto C. (2004). Molecular mechanisms of neurotoxicity of pathological Prion protein. ***Curr. Mol. Med***. 4:397-403. *

111. **Hetz C**., Russelakis, M., Maundrell, K. Castilla, J. and Soto, C. (2003). Caspase-12 and endoplasmic reticulum stress mediate neurotoxicity of pathological prion protein**.** ***EMBO J***. 22:5435-5445. *

112. Commented in *Science,* STKE (2003) 302:1007. Prions stress out the ER.

113. **Hetz, C.**, Maundrell, K. and Soto, C. (2003). Is loss of function of the prion protein the cause of Prion Disorders? ***Trends Mol. Med***. 9:237-243.*

114. **Hetz, C**. and Soto, C. (2003). Prion Misfolding and Disease: The Case of Prion Protein. ***Cell. Mol. Life Sci.*** 60:133-1432.*

115. **Hetz C**., Benavent, S. Bieler, S. and Soto, C. (2003). Prion Protein Misfolding and Brain Degeneration. ***Curr. Med. Chem***. 3:137-147.*

116. **Hetz, C**., Hunn, M., Rojas, P. Leyton, L., and Quest, A. F. (2002). Caspase-dependent Initiation of Apoptosis and Necrosis by the Fas Recetor: A Role for the Lipid Second Messenger Ceramide in Initiation of FasL-induced Necrosis***. J. Cell Sci***. 115: 4671-83.*

117. Commented in *J. Cell. Sci.* (2002) 115:e2304. Apoptosis vs necrosis: ceramide decides it. and in *Science*, STKE (2002), Issue 158: 414. A Back-up death plan.

118. **Hetz**, **C.** Bono, M., Barros, F. and Lagos, R. (2002). Microcin E492, a Channel-forming Bacteriocin from *Klebsiella pneumoniae*, Induces Apoptosis in Some Human Cell Lines. ***Proc. Natl. Acad. Sci USA***. 99:2696-2701. *

119. Leyton, L., Schneider, P., Labra, C., Ruegg, C., **Hetz**, **C**., Quest, A. and Brown C. (2001). Thy-1 binds to the integrin β3 on astrocytes and triggers formation of focal contact sites. ***Curr. Biol.*** 11:1028-38.*

120. Barros, F., Stutzin, A., Calixto, A., Catalán, M., Castro, J., **Hetz, C.,** and Hermosilla, T. (2001). Non-selective Cation Channels as Effectors of Free Radical-induced Liver Cell Necrosis. ***Hepatology***. 33:114-22.*

121. Lagos, R., Baeza, M., Corsini, G., **Hetz, C.**, Strahsburger, E., Castillo J., Vergara C., and Monasterio O. (2001). Structure, Organization and Characterization of the Gene Cluster Involved in the Production of Microcin E492, a Channel-Forming Bacteriocin. ***Mol. Microbiol.*** 42: 229-244.*

Book chapters

Bargsted L., Vidal R., **Hetz C**., and Matus M. (2015) Dual role of autophagy in neurodegenerative diseases: The case of amyotrophic lateral sclerosis. **Springer editorial**. Book entitled "Toxicity and Autophagy in Neurodegenerative Disorders". 63-78 *#

Nassif M, Danilo Medinas, Karen Castillo, Camila Gherardelli, and **Claudio Hetz**. (2013). When the good turns bad: Challenges in the targeting of autophagy in neurodegenerative disease. Book Chapter 4-volume series, "Autophagy: Cancer, Other Pathologies, Infection, Inflammation and Immunity" ***Elsevier Publishing Company.*** *In press.*

Galleguillos D., Matus S. Valenzuela V., Valdes P., Martinez A., Nassif M., Torres M., Martinez G., and **Hetz C**. (2009). Targeting endoplasmic reticulum stress pathways to alleviate neurological disorders associated with protein misfolding. E-book series. ***Bentham Science Publishers***.

Rojas D., Caballero, B., Zamorano S., Lisbona F., and **Hetz C.** (2010). Alternative Functions of the BCL-2 Protein Family at the Endoplasmic Reticulum. ***Bioscience publishers. Adv Exp Med Biol.*** 2010;687:33-47.

Hetz C. BCL-2 protein family. (2010). Essential regulators of cell death. Preface. ***Bioscience publishers. Adv Exp Med Biol.*** 2010;687:vii-viii.

Matus S., Thielen P., Nassif M., Torres M., and **Hetz C** (2008) Targeting stress pathways to treat neurological disorders linked to protein misfolding. *Protein Misfolding.* ***Nova Science Publishers***, Inc. Editor Cian B. O'Doherty and Adam C. Byrne *#

Russelakis-Carneiro, M., **Hetz, C**., Castilla, J. and Soto, C. (2004) Neurodegeneration induced by prion protein misfolding. In *"Neuroprotection: Models, Mechanisms, Therapies"* M. Bahr (Ed.). ***Wiley-VCH***.*

Morales R., **Hetz C.** and Soto C. (2004). Signaling Pathways Controlling Prion Neurotoxicity: Role of Endoplasmic reticulum stress-mediated Apoptosis. *Neurodegeneration in Prion Disorders.* ***Klewer.*** Editor: David Brown. *

Books

Book editor: e-book "***Protein Misfolding Disorders: A Trip into the ER***". 2009. Bentham Science Publishers. http://www.bentham.org/ebooks/9781608050130/index.htm

Book editor: "***BCL2 Protein Family: Functions beyond Apoptosis"***. 2010. Bioscience publishers. http://www.landesbioscience.com/books/iu/id/3413/

Papers under revision or invited

Ute Woehlbier, Paloma Gonzalez-Perez1, Alicia Colombo, Catherine Andreu, Mauricio Torres, Vicente Valenzuela, Alvaro Diaz, Ricardo Armisen, Alfredo Sagredo, Johnny Salameh, Ru-Ju Chian, Peter Sapp, Karina Palma, Miguel L. Concha, Robert H. Brown and **Claudio Hetz** (2015). Mutations in Protein Disulfide Isomerases Contribute to the Development of ALS. ***Genes Dev*** *under revision*

Gabriela Martínez, René L. Vidal, Felipe G. Serrano, Craig Wirth, Pablo Mardones, Claudia Molina, Pamela Valdés, Peter Thielen, Cecilia Hidalgo, Bernard L. Schneider, Bredford Kerr, Jose Luis Valdés, Nibaldo C. Inestrosa, Laurie H. Glimcher and **Claudio Hetz**. (2015) Regulation of memory formation by the transcription factor XBP1. ***Nature Communications***. Under revision.

Rojas DR and **Hetz C.** (2014). Dynamic regulation of the UPR, novel concepts. ***Cell Res.*** Invited review.

Hetz C and Papa F. (2015) Cell fate under ER stress. ***Molecular Cell*** Under preparation.

Klionsky and 1200 (**Hetz C**) others (2015) Guidelines for the Use and Interpretation of Assays for Monitoring Autophagy. ***Autophagy.*** Invited article.

INTELECTUAL PROPERTY Files: PATENTS

Claudio Hetz and Laurie Glimcher, application HUI-073-1 (2008). MODULATION OF NEURODEGENERATIVE DISEASE BY MODULATING XBP-1 ACTIVITY

CURRENT RESEARCH SUPPORT
NATIONAL

- NAME: Chilean government funding agency FONDECYT.
  TITLE: The UPRosome: novel regulatory checkpoints and physiological outputs.

ROLE: **Principal investigator**. ID**:** FONDECYT # 1140549. ID: FONDECYT. Project ranked **number one** in the study section. 2014-2017.

- NAME: Chilean government, Millennium Scientific Initiative (Program grant).
  TITLE: Biomedical Neuroscience Institute (BNI). ID: P09-015-F.
  ROLE: **Deputy Director**. 2011-2016.

- NAME: Chilean government funding agency FONDEF.
  TITLE: UPRplus: A novel gene therapy to treat Parkinson´s disease.
  ROLE: **Principal investigator**. ID: D11I1007. 2012-2015.

- NAME: Ring Initiative, Chile.
  TITLE: Neuronal network initiative: Understanding selective neuronal vulnerability in neurodegenerative diseases. ROLE: **Associate investigator**. ID: ACT1109
  ID: ACT1109. 2013-2015.

- NAME: CONICYT-Cooperation grant Chile-EEUU
  TITLE: GENE THERAPY STRATEGY TO TARGET THE UNFOLDED PROTEIN RESPONSE IN ALS.
  ROLE: **Principal investigator**. ID: USA2013-0003. 2013-2016.

- NAME: Fundacion COPEC-UC.
  TITLE: Identification of neuroprotective compounds from Chilean endogenous plants.
  ROLE: **Principal investigator**. 2014-2015.

INTERNATIONAL

- NAME: The Michael J. Fox Foundation for Parkinson's Research, USA TITLE: Targeting the ER stress sensor PERK for the treatment of Parkinson´s disease. Role: **Principal Investigator.** ID: Target Validation grant. 2014-2015.

- NAME: Muscular Dystrophy Association, USA.
  TITLE: A role of ER stress in wild-type SOD1 misfolding: A model for sALS?
  Role: **Principal Investigator** and project manager. ID: # MDA218655. 2012-2015

- NAME: ALS Therapy Alliance, USA.
  TITLE: Defining the function of protein Disulfide Isomerases in ALS
  Role: **Principal Investigator**. 2012-2015

- NAME: Alzheimer's Association, USA
  TITLE: Defining the role of the Unfolded Protein Response in Alzheimer s Disease
  ROLE: **Principal Investigator**. 2012-2014.

- NAME: Awarded with a gift from Christopher Reeve Spinal Cord Injury and Paralysis Foundation, USA
  TITLE: targeting ER stress in Spinal Cord Injury
  ROLE: **Principal Investigator**. 2015.

- NAME: Frick Foundation, Switzerland. TITLE: Defining the contribution of ER proteostasis disturbances to ALS. Role: **Principal Investigator.** ID: Target Validation grant. 2015-2016.

PAST RESEARCH SUPPORT

- NAME: Chilean government funding agency FONDECYT.
  TITLE: Defining the contribution of the disulfide isomerase ERp57 to the pathogenesis of Prion-related disorders. ROLE: **Principal investigator**.

ID: FONDECYT # 1100176. Project ranked **number one** in the study section. 2010-2014.

- NAME: FONDEQUIP
  TITLE: Cellomics: An automatized platform for high throughput microscopy with biotechnological potential.
  ROLE: **Principal investigator**. ID: EQM120164. 2012

- NAME: The Michael J. Fox Foundation for Parkinson's Research, USA
  TITLE: Targeting the unfolded protein response (UPR) transcription factor XBP1 to alleviate neurodegeneration triggered by alpha-synuclein
  Role: **Principal Investigator**. ID: Target Validation grant. 2012-2013.

- NAME: North American Spine Society (NASS), USA
  TITLE: Defining the role of the endoplasmic reticulum (ER) stress and the UPR in spinal cord injury
  Role: **Principal Investigator**. ID: Research grant. 2011-2012.

NAME: CHDI Foundation, Inc, Research Grant, USA
TITLE: Defining the role of the Unfolded Protein Response in Huntington's disease in vivo.
ROLE: **Principal Investigator**. 2008-2010.

NAME: The Michael J. Fox Foundation for Parkinson's Research, USA
TITLE: Targeting the Unfolded Protein Response (UPR) transcription factor XBP-1 to treat Parkinson's
Role: **Principal Investigator**. ID: Target Validation grant.2010-2011.

NAME: Alzheimer's Association, USA
TITLE: Defining the role of the Unfolded Protein Response in Alzheimer s Disease
ROLE: **Principal Investigator**. ID: NIRG-10-173294. 2010-2012.

NAME: FONDAP (Program grant)
TITLE: FONDAP Center for Molecular Studies of the Cell (CEMC)
ROLE: **Principal investigator.** ID: FONDAP #15010006. 2007-2012.

NAME: Chilean government, Millennium Scientific Initiative (Program grant).
TITLE: Millennium Nucleus for Neural Morphogenesis (NEMO).
ROLE: **Associate investigator.** ID: Nucleo Milenio # P07-048-F. 2009-2011.

NAME: Muscular Dystrophy Association, USA.
TITLE: Targeting Autophagy for the removal of mutant SOD1 in ALS.
Role: **Principal Investigator**. ID: # MDA10036. 2008-2010

NAME: FONDECYT Chile
TITLE: The tumor suppressor activity of Caveolin 1 is associated with an inhibition of the UPR
ROLE: **Co-investigator.** ID: FONCECYT.# 1090071. 2009-1013.

NAME: GENZYME, USA.
TITLE: Targeting BECLIN-1 to modulate autophagy mediated degradation of mutant SOD1 and other disease related misfolded proteins.
ROLE: **Principal investigator.** SOURE: Sponsored Research Agreement. 2010-2011.

NAME: ICGEB, International Center for Genetic Engineering and Biotechnology. Italy.
TITLE: Role of the Unfolded Protein Response (UPR) in tumor suppression by caveolin-1.
Role: **Principal Investigator**. 2009-2011. ID: # CRP/CHI08-03. 2009-2011.

NAME: Chilean government funding agency FONDECYT.
TITLE: Regulation of the Unfolded Protein Response (UPR) by the stress sensor IRE1α and its role in neurological disorders. ROLE: **Principal investigator**.

SOURCE and ID: FONDECYT # 1070444. **Project Ranked number one** in the study section. 2007-2010.

NAME: The Michael J. Fox Foundation for Parkinson's Research, USA
TITLE: A role of the UPR in Parkinson's disease
Role: **Principal Investigator**. 2008-2009.

NAME: High Q Foundation, discovery initiative, USA
TITLE: A role of Endoplasmic Reticulum Stress in Huntington's Disease.
ROLE: **Principal Investigator**. 2007-2008.

NAME: National Parkinson Foundation, USA
Title: Defining the contribution of endoplasmic reticulum (ER) stress in Parkinson's disease.
Role: **Principal Investigator**. 2008-2009.

NAME: GENZYME, USA.
TITLE: Targeting Autophagy for the treatment of Protein Conformational Disorders affecting the nervous system. ROLE: **Principal investigator.** 2008-2009.

NAME: Chilean government funding agency FONDECYT.
TITLE: Regulation of neuronal apoptosis by Abl in Alzheimer's disease. ROLE: **Co- investigator.** PI: Alejandra Alvarez (Catholic University of Chile). ID: FONDECYT # 1080221. 2008-2012.

REVIEWER or EDITOR

- Invited reviewer for *Science, Cell, Nature, Nature Communication, Nature Cell Biology, Science Translational Medicine, Science Signaling, PLoS Biology, PLoS One, The EMBO Journal, Journal of Neuroscience, Molecular Cell, Cell Death and Differentiation, Apop*tosis, *Cell Metabolism, Proceeding of the National Academy of Science USA, The FASEB Journal, Cell Death and Disease, European Journal of Neuroscience, Cellular Microbiology, European Journal of Cell Biology, Human Molecular Genetics, EMBO Reports, Journal of Neurochemistry, Leukemia Research, Experimental Gerontology, Journal of the American Society of Nephrology, Biological Research, Oncogene, Neuroscience Letters, Brain research, Journal of the American Society of Nephrology, BBA - Biomembranes, Cells, Antioxidant and Redox Signaling, Cellular and Molecular Life Sciences, ACS Chemical Neuroscience, and Current Molecular Medicine.*
- External reviewer for the Health, Welfare and Food Bureau (HWFB) of the Hong Kong Government.
- Editor special editor *Current Opinion Cell Biology 2011*
- Associate Editor of the *Current Molecular Medicine*
- Editor of E-book series. *Bentham Science Publishers*.
- Editor of book from *Bioscience Publishers*.
- External reviewer for Chilean government's grant agency FONDECYT.
- External reviewer for Wellcome Trust/DBT India Alliance
- External reviewer Alzheimer's Association, USA.

THESIS ADVISOR

(i) Post-doctoral fellows

Dr. Soledad Matus (2007-2012); Dr. Danny Galleguillos (2008-2009); Dr. Rene Vidal (2008-2013); Dr. Andrea Paula (2007-2010; co-advisor); Dr. Karen Castillo (2008-2013); Dr. Gonzalo Encina (2009-2011); Dr. Ute Woehlbier (2010-2014); Dr. Gabriela Mercado (2011-present); Danilo Bilches (2012-present); Diego Rojas (2012-present), Nestor Guerrero (2012-present), Claudia Duran (2013-present); Pablo Mardones (2013-present); Paula Huerta (2014-present); Gabriela Martinez (2014-present).

(ii) PhD students

A. Thesis under development (Ph.D. candidates) or finished:

- **Diego Rojas**. (2008-2012) "TMBIM3/GRINA: A Gene regulated by the response misfolded proteins (UPR) which inhibits apoptosis through modulation of calcium homeostasis". *Ph.D. in Biochemistry, University of Chile.* **Awarded as Best PhD thesis of Chile, Allende and Connelly Foundation, Chile 2013.**
- **Clara Quiroga** (2006-2010) "Role of protein HERP and its post-translational modifications in cell death induced by stress of the endoplasmic reticulum". *Ph.D. in Biochemistry, University of Chile.* (co-advisor).
- **Melissa Calegaro** (2007-2012) "Mechanism of the increased autophagy levels in a model of familial amyotrophic lateral sclerosis: interaction between mutant SOD1 and Beclin-1/Bcl-2 autophagy regulatory complex". *PhD. Biomedical Sciences, University of Chile. (Finished)*
- **Pamela Valdés** (2008-2013) "Pathological effect of endoplasmic reticulum stress in Parkinson's disease". *PhD. Cellular and Molecular Biology, University of Chile.*
- **Mauricio Torres** (2007-2013) "Role of the disulfide isomerase ERp57 in the pathogenesis of Prion-related disorders". *PhD. Biomedical Sciences, University of Chile*.
- **Gabriela Martínez** (2010-2014) "Role of XBP1 on NMDA receptor transport regulation through KIF 17" . *Ph.D Biomedical Sciences, University of Chile*.
- **Maria Inés Díaz** (2008-present) "Role of the response to misfolded proteins in the activity of suppressor protein caveolin-1". *Ph.D. in Biochemistry, University of Chile*.
- **Fernanda Lisbona** (2010-present)." RECS1 study the role of a BI-1 orthologue in the regulation of autophagy" Ph.D Farmacology, University of Chile. **Awarded with the Loreal Woman in Science Price (2011) and the RELAB Prize (2012).**
- **Victor Hugo Cornejo**, 2011-present. "Role of the UPR in Alzheimer´s disease". *PhD in Biomedical Sciences, University of Chile.*
- **Hery Urra** (2011-present). "Role of IRE1 in cell migration". *PhD. Biomedical Sciences, University of Chile.*
- **Estephanie Dufei** (2012-present) Role of the UPR in DNA damage responses. *PhD. Biomedical Sciences, University of Chile.*
- **Vicente Valenzuela** (2012-present). Gene therapy to target ER stress in ALS. *PhD. Biomedical Sciences, University of Chile.*
- **Alexis Martinez** (2012-present). Role of Abl-c and ER stress in ALS. PhD in Cellular and Molecular Biology, P. Catholic University of Chile (Co-mentored with Dr Alejandra Alvarez).

B. PhD. Thesis projects under preparation:

- **Philippe Pihan** (2012-present) PhD. Biomedical Sciences, University of Chile.
- **Maritza Oñate** (2013-present). PhD in Neurosciences, P. Universidad Católica de Chile.
- **Denisse Sepulveda** (2013-present). PhD. Biomedical Sciences, University of Chile.

(ii) Master's students

A. Thesis under development or finished:

- **Peter Thielen (2010-2011):** Master in Biotechnology, Harvard University, USA. Awarded with the Dean's Prize for Outstanding ALM Thesis.
- **Vicente Valenzuela** (2009-2010) "Role of the Endoplasmic Reticulum Stress and the Unfolded Protein Response in Locomotor Recuperation in Spinal Cord Hemisected Mice". *Master in Biological Sciences, Faculty of Sciences, University of Chile.*

Awarded as Best Master´s thesis of Chile, Chilean Cell Biology Society, Chile 2012.

- **Fernanda Lisbona** (2007-2008) "BAX Inhibitor-1 negatively regulates stress sensor IRE1 alpha". *Master in Biological Sciences, Faculty of Sciences, University of Chile.*
- **Andrés Henriquez** (2009-2012) "Determination of the Impact of the composition of particulate matter air in their lung toxicity*". Master in Biological Sciences, Faculty of Sciences, University of Chile.*
- **Maritza Onate** (2011-present) "The role of the unfolded protein response in axonal regeneration after sciatic nerve injury". *Master in Biological Sciences, Faculty of Sciences, University of Chile.*

- **Valentina Castillo** (2013-present) *Master in Biological Sciences, Faculty of Sciences, University of Chile.*
- **Leslie Bargsted** (2013-present) *Master in Biological Sciences, Faculty of Sciences, University of Chile.*

B. Master thesis projects under preparation:

- Pablo Rozas (2014-present)**.** *Master in Biological Sciences, Faculty of Sciences, University of Chile.*

(iv) Undergraduate Students

- **Sebastian Zamorano** (2007-2009) "Characterization of a new way of apoptosis essentially independent of BAX, BAK AND cyclophilin D". *Molecular Biotechnology Engineering, Faculty of Science, University of Chile.*
- **Andrés Henriquez** (2007-2009) "Implementation of a method for evaluating the toxicological response caused by the atmospheric particulate matter using rats as a model study". *Molecular Biotechnology Engineering, Faculty of Science, University of Chile.*
- **Vicente Valenzuela** (2008-2009). "Characterization of the Activation of the Unfolded Protein Response by Spinal Cord Hemisection in Mice". *Molecular Biotechnology Engineering, Faculty of Science, University of Chile.*
- **Amparo Zuleta** (2010-2011) "Using adeno-associated viral vectors to study the impact of the transcription factor XBP-1 in a mouse model of Huntington's Disease". *Molecular Biotechnology Engineering, Faculty of Science, University of Chile.*
- **Catherine Andreu** (2011-2012) "Effect of ERp57 deficiency in the central nervous system of a murine model" *Molecular Biotechnology Engineering, Faculty of Science, University of Chile.*
- **Leslie Bargted** (2012-2013) "characterization of new transgenic model of amyotrophic lateral sclerosis, possible alteration of endoplasmic reticulum homeostasis induced protein TDP-43 in its mutant form". *Molecular Biotechnology Engineering, Faculty of Science, University of Chile.*
- **Valentina Castillo** (2012-2014) "Modulating effect ERp57 in survival of dopaminergic neurons in the pharmacological mouse model of Parkinson disease". *Molecular Biotechnology Engineering, Faculty of Science, University of Chile.*
- **Camila Gherardell** (2013) "Role of BCI1 in the control of autophagy. *Biotechnology*, Universidad Mayor.
- **Miguel Gonzalez** (2014-present) "Role of BCI1 in the control of autophagy. *Biotechnology*, Universidad Mayor.

(v) Current unit of investigation.
Martin Sepulveda, Molecular Biotechnolgy Engeneer, University of Chile.
Fernando Pasten, Biochemistry, University of Chile.

(vi) Current staff and laboratory technicians with degree of Biochemistry or Biology
Vanessa Valledares (Assistant), Daniela Concha (lab manager), Javiera Ponce (Veterinary) Natalia Muñoz, Sandra Espinoza,Claudia Lucero, and Carolina Jerez (lab tech).

(vi) International rotation students.
- Andrew Foley (2014). Post-Baccalaureate Researcher Franklin and Marshall College, USA
- Oriane Fracchia (2014). Master in Aging and Longevity at University Pierre and Marie Curie, Paris, France.
- Cynthia Lefevbre (2013). Master in Aging and Longevity at University Pierre and Marie Curie, Paris, France.
- **Santeri Kiviluoto** (2012). PhD in Cell Biology. Dept. Cellular and Molecular Medicine, Leuven, Belgium.

SELECTED TEACHING EXPERIENCE

-Professor seminar course at the Ph.D. on Biomedical Sciences: (i) Mechanism of adaptation to Cellular Stress and (ii) Protein Misfolding Disorders.

-Invited professor to different courses at the Ph.D. program in Biomedical Sciences, PhD on Biochemistry, PhD in Medical Sciences, PhD on Molecular and Cellular Biology and Neuroscience, University of Chile:

Invited Professor also at PhD programs at Andres Bello University, Universidad de Concepción, Universidad Austral de Chile, and the P. Catholic University of Chile.

SELECTED SYMPOSIA PARTICIPATION

Hetz C. 2013 Protein folding stress in neurodegenerative disease: an interplay between ER stress and autophagy. **Seminar UGent – VIB** Ghent ,Belgica. January 13-22.

Hetz C. 2013. Novel function of the UPR transcription factor XBP1 in the regulation of learning and memory **"FASEB Science Research Conference: From Unfolded Proteins in the ER to Disease".** Vermont, USA. June 16-21. Speaker.

Hetz C. 2013. Mutations in protein disulfide isomerases contribute to the development of ALS. **10th Calreticulin workshop**. Alberta, Canada. April 10-13. Speaker.

Hetz C. 2013. The Unfolded Protein response (UPR) in neurodegenerative diseases. **Seminar guess speaker University of Alberta**. Edmonton, Canada. April 8-9. Speaker.

Hetz C. 2013. The IRE1 interactome: fine tunning of UPR signaling. **Gordon Research: Stress proteins in growth , development & disease**. Vermont, USA. July 7-12. Speaker

Hetz C. 2013 "Targeting the unfolded protein response transcription factor XBP1 to alleviate neurodegeneration triggered by alpha-synuclein." **M.J.Fox Foundation final assessment grant meeting** New York, USA. August 7-11

Hetz, C. 2013. Protein folding stress in neurodegenerative disease: an interplay between ER stress and autophagy. **Neurotoxicity society meeting: Mechanisms of neurodegenerative disorders.** Valdivia, Chile. March 21-24. Speaker

Hetz C. 2012. Protein folding stress in neurodegenerative disease: an interplay between ER stress and autophagy. **Congress 22nd IUBMB and 37th FEBS. Sevilla, España**, September 4-9.

Rojas-Rivera, D; Armisen, R; Martinez, G; Kiviluoto, S; Rodriguez, D; Patron,M; Rizzuto, R; Concha, M; Sierralta, J; Stutzin,A; **Hetz, C.** 2012 TMBIM3/GRINA is a novel unfolded protein response (UPR) target gene that controls apoptosis through the modulation of ER calcium homeostasis. **Congress 22nd IUBMB and 37th FEBS.** Sevilla, España, September 4-9.

Woehlbier, U;Torres M; Valenzuela, V; Hetz, C. Mutations in Protein Disulfide Isomerases are linked to ALS pathology. **EMBO/EMBL Symposium Qualoty Control from Molecules to organelles**. Heidelberg, Alemania. September 19-22.

Vidal, R; Zuleta, A; Figueroa, A; Molina, C; and **Hetz, C.** 2012 Targeting the UPR transcription factor XBP1 protects against Huntington's disease in vivo. **Neurodegeneration conference ZING**. Cancun, Mexico. November 27- December 1.

Martínez, G; Vidal, R; Wirth, C; Pihán, P; **Hetz, C.** 2012 Possible role of the UPR transcription factor XBP1 in the regulation of memory formation. **Neurodegeneration conference ZING**. Cancun, Mexico. November 27- December 1.

Castillo, K; Nassif, M; Valenzuela, V; Rojas,F; Matus, S; Mercado, G; Court, F.A; and **Hetz, C**. 2012 Trehalose protects against amyotrophic lateral sclerosis progression by enhancing autophagy. **Neurodegeneration conference ZING**. Cancun, Mexico. November 27- December 1.

Torres, M; Woehlbier, U; Andreu, C; Solda, T; Molinari, M; **Hetz, C**. 2012 The protein disulfide isomerase family member ERp57 modulates prion protein turnover. **Neurodegeneration conference ZING**. Cancun, Mexico. November 27- December 1.

Hetz C. 2012. TMBIM3/GRINA is a novel unfolded protein response (UPR) target gene that controls apoptosis through the modulation of ER calcium homeostasis. **Gordon Research Conference: Cell Death**. Lucca, Italy, July 15-20. Speaker.

Hetz C. 2012. Protein folding stress in neurodegenerative disease. IX Workshop on the Molecular Biology of Stress Responses. May 27-30, Porto Allegre, Brazil. Speaker.

Hetz C. 2012. Unfolded Protein Response (UPR) in neurodegenerative diseases. **Neurodegeneration: Opportunities for Collaboration Across Disease-Specific Research and Development Communities** - *A Workshop.* April 30- May 1, Washington DC, USA. Speaker.

Hetz C. 2011**. Parkinson's Disease Therapeutics Conference.** Targeting the Unfolded Protein Response (UPR) transcription factor XBP-1 to treat Parkinson's Disease. New York, USA, October 26. Speaker.

Hetz C. 2011. **Latin America Huntington' s Disease Workshop.** Functional Role of the unfolded protein response in Huntington's disease. October 17-19, Santiago, Chile. Speaker.

Rodríguez D, Zamorano S, Lisbona F, Rojas D, Arminsen R, Cubillos-Ruiz J, Irrazabal T, Gonzalez-Billault C, and **Hetz C.** 2011. BH3-only proteins control the sustained signaling of the Unfolded Protein Response sensor IRE1α. Signaling in cell death survival, proliferation and degeneration. Queens Collage Foundation. June 10-13, Sao Paulo, Brazil. *Speak**er***

Rodríguez D, Zamorano S, Lisbona F, Rojas D, Arminsen R, Cubillos-Ruiz J, Irrazabal T, Gonzalez-Billault C, and **Hetz C**. 2011. BH3-only proteins control the sustained signaling of the Unfolded Protein Response sensor IRE1α. **FASEB Research Conferences** Vermont Academy From Unfolded Proteins in the Endoplasmic Reticulum to Disease. June 12-17, Vermont, Canadá. *Speaker*

Vidal R, Figueroa A, Court F, Thielen P, Wirth C, Cuervo AM, Glimcher L.H., and **Hetz C**. 2011 D434 Targeting the UPR transcription factor XBP1 protects against experimental Huntington's disease by enhancing mutant Huntington clearance by autophagy. 8th IBRO World Congress of Neuroscience. July 14-18, Florence, Italy.

Hetz C. (2011) Homeostatic Connection between the Unfolded Protein Response (UPR) and Autophagy in Neurodegeneration.Keystone meeting on autophagy. **Keystone meeting** on Autophagy. March 27 - April 1, Whistler, Canada. *Speaker*

Castillo, K; Caballero, B; Nassif, M, Matus S., and **Hetz, C.** 2010. Targeting the autophagy machinery decreases mutant SOD1 aggregation in a cellular model of Amyotrophic Lateral Sclerosis. **EMBO workshop** Proteolysis and Neurodegeneration, 4 - 7 May, Madrid, Spain. ***Speaker.***

Hetz C. 2010. Homeostatic balance between the Unfolded Protein Response (UPR) and autophagy in the nervous system: lessons from ALS. **Gordon Conference**: Autophagy In Stress, Development & Disease. Lucca (Barga), Italy. April 25-30, ***Speaker.***

NASSIF M., Matus S., Castillo K., Brown R.H., and **Hetz C**. 2010. A role of BECLIN-1 in the regulation of autophagy in Amyotrophic lateral sclerosis. **Gordon Conference**: Autophagy In Stress, Development & Disease. Lucca (Barga), Italy. April 25-30,

Matus S., Thielen P, M Nassif, Court F., Cuervo AM., Martinez G., Kiffin R., R.H. Brown, Glimcher L., and **Hetz C.** 2009. XBP-1 deficiency in the nervous system protects against amyotrophic lateral sclerosis by increasing autophagy. **Gordon Conference** Stress Proteins in growth, Development and Disease, USA.

Lisbona F, Rojas D., Zamorano S., Thielen P., Walter P., Reed JC, Glimcher L. and **Hetz C**. 2009. BAX Inhibitor-1 is a negative regulator of the ER stress sensor IRE1 and is a component of the *UPRosome*: A new function beyond apoptosis. **Key Stone Meeting** on Cell death Pathways. Canada.

Matus S., Calegaro M, Martinez G., Torres M., Brown R., Glimcher L. and **Hetz H**. 2009. Stress Responses in Protein Misfolding Disorders: An Intimate Crosstalk Between the UPR and Autophagy. 8th International Calreticulin Workshop. January 6-8. Vina del mar, Chile. ***Speaker***

M. Calegaro, S. Matus, P. Thielen, L. Glimcher and C. **Hetz C**. 2008**.** XBP-1 deficiency protects against Amyotrophic Lateral Sclerosis due to increased autophagy. I Congress IBRO/LARC of Neurosciences for
Latin America, Caribbean and Iberian Peninsula. September 1-4. Buzios, RJ, Brazil.

F. Lisbona, D. Rojas, P. Thielen, C. Kress, J. Reed, P. Walter, L. Glimcher and **C. Hetz**. 2008. BAX Inhibitor-1 is a negative regulator of the ER stress sensor IRE1: A new functions beyond apoptosis. **Gordon Conference:** Molecules That Specify The Variety Of Cell Death Mechanisms. July 6-11. Lucca (Barga), Italy.

S. Matus, P. Thielen, M. Calegaro, R. Brown, L. Glimcher and **C. Hetz.** 2008. XBP-1 deficiency protects against Amyotrophic Lateral Sclerosis due to increased autophagy. **Gordon Conference:** Molecules That Specify The Variety Of Cell Death Mechanisms. July 6-11. Lucca (Barga), Italy.

S. Zamorano, F. Lisbona, E. Cheng and **C. Hetz**. ER stress induces mitochondrial-mediated apoptosis independent of BAX and BAK and cyclophilin D: A new intrinsic death pathway?. **Gordon Conference:** Molecules That Specify The Variety Of Cell Death Mechanisms**.** July 6-11. Lucca (Barga), Italy.

C. Hetz, P. Thielen, S. Matus, M. Nassif, R.H. Brown and L. Glimcher. 2008. XBP-1 deficiency in neurons protects against amyotrophic lateral sclerosis by increasing autophagy. Sporadic Neurodegeneration: Genes, Environment and Therapeutic Strategies. july 31-august 01 . Boston, USA.

S. Matus, S. Korsmeyer, L. Glimcher and **C. Hetz**. "The proapoptotic BCL-2 family member BIM, mediates motoneuron loss in a model of amyotrophic lateral sclerosis". Annual meeting of The Biology Society of Chile. October, 2007.

F. Lisbona, M. Torres, S. Matus, C. Soto and **C. Hetz**. "A role of the Unfolded Protein Response (UPR) and Endoplasmic Reticulum stress in Prion-related disorders". Annual meeting of The Biology Society of Chile. October, 2007.

Hetz C. Thielen P., Fisher J., Korsmeyer S. and Glimcher L. 2007. The Pro-apoptotic BCL-2 Family Member BIM Mediates Motoneuron Loss in a Model of Amyotrophic Lateral Sclerosis. Keystone meeting in Apoptotic and Non-apoptotic Cell Death Pathways. 15-20 April, Monterey, USA, ***Speaker***

Soto, C. Morales, R., Abid, A., and **Hetz, C**. 2007. Mechanism of Prion Neurotoxicity. Keystone meeting in Apoptotic and Non-apoptotic Cell Death Pathways. 15-20 April, Monterey, USA, ***Speaker***

Soto, C. Morales, R., Abid, A., and **Hetz, C.** 2006. Prion protein misfolding and the mechanism of neurodegeneration. ***Cold Spring Harbor Laboratory.*** May, New York, USA. ***Speaker***

Hetz, C. Bernasconi, P. Fisher, Lee, A., Wei, G., Korsmeyer, S. and Glimcher L. 2006. Proapoptotic BAx and Bak modulate the unfolded protein response through a direct interaction with Ire1a. ***Keystone symposia*** Protein Misfolding Diseases: Mechanisms of Misfolding, Pathology and Therapeutic Strategies***.*** 21-26 Febr. Colorado, USA. ***Speaker***

Hetz C. Soto C. and Korsmeyer S. 2005. Endoplasmic reticulum stress mediates the neurotoxicity of pathological prions. ***Cold Spring Harbor Laboratory.*** Sep, New York, USA. ***Speaker***

Hetz, C. and Korsmeyer, S. 2005. A role of the Bcl-2 protein family on endoplasmic reticulum physiology. Mechanisms of Cell Death: Molecular Insights and Therapeutic Perspectives. 13-16 Apr. Chile. ***Apeaker***

Hetz, C. and Soto C. 2004. Prions stress out the ER: Mechanism of neuronal degeneration in prion disorders. Institute for TSE Research. Febr, Edinburgh, Scotland. ***Speaker***

Hetz, C., Russelakis M., and Soto C. 2003. The pathological prion protein induces apoptosis by disruption of calcium homeostasis and activation of caspase-12. Apoptosis 2003*: From signaling pathways to therapeutic tools.* Jan. Luxemburg, ***Speaker***

Hetz, C., Russelakis M., Castilla J., Maundrell K. and Soto C. 2003. PrP^{SC} toxicity depends on ER-stress and caspase-12 activation. *Annual meeting of the Chilean Society of Biochemistry and Molecular Biology*, Sep. Chile. ***Invited speaker***.

Hetz, C., Hunn, M., Rojas, P., Leyton, L., and Quest, A. 2002. Fas Receptor-mediated necrotic cell death in lymphoid cells: A role for ceramide? *International Workshop in Cancer, Aging and Apoptosis.* Sep. Geneva, Switzerland. ***Speaker***

Hetz, C. and Soto, C. 2002. Diagnosis of TSE by Cyclic amplification of Protein Misfolding. *Blood Product Safety and transmissible Spongiform Encephalopathies.* Febr. Bergen, Norway. ***Speaker***

Hetz, C., Bono, M., Barros, F. and Lagos, R. 2000. The channel forming bacteriocin Microcin E492 induces apoptosis on different human cell lines. ***Cold Spring Harbor Laboratory***. Aug. New York, USA

Hetz, C., Hunn, M., Rojas, P. and Quest, A. F. 2000. A role for ceramide in Fas ligand induced caspase-dependent necrosis of murine A20 B lymphoma cells. *International Symposia: Cellular and Molecular Aspects of the Birth, Life and Death of Nervous System.* Sep. Chile. ***Speaker***

Hetz, C., Bono, M., Barros, F. and Lagos, R. 1999. Characterization of the cytotoxic effect of microcin E492 over different human cell lines: A model in the study of cell death. Biological Research, vol 32: 2-3. XLII *Annual meeting of the Chilean Biological Society.* ***Speaker***